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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,588	03/09/2006	Taro Yoshikawa	126835	7199

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,588	YOSHIKAWA ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 9-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the national stage entry of PCT/JP04/11462, filed 10 Aug 2004; and claims benefit of foreign priority document JAPAN 2003-292135, filed 12 Aug 2003; currently an English language translation of this foreign priority document has not been filed.

This Office Action is responsive to Applicant's amendment filed 03 Dec 2007, wherein claim 1 was amended, claims 2 and 5-8 were cancelled, and new claims 9-14 were submitted.

Claims 1, 3, 4 and 9-14 are pending in the current application. Claims 11-14, drawn to non-elected inventions, are withdrawn. Claims 1, 3, 4, 9 and 10 are examined on the merits herein.

Election/Restrictions

Newly submitted claims 11-14 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The inventions of original claims 1-8 and newly submitted claims 11-14 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the product as claimed can be used in the materially

different process of using that product by adding it to food as a flavoring or sweetening agent.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-14 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Objections Withdrawn

Applicant's amendment, filed 03 Dec 2007, with respect to the objections regarding minor informalities in the specification have been fully considered and found to be persuasive to remove the objection as the amendment addresses the issues raised in this objection. Therefore this objection is withdrawn.

The following rejection has been modified in response to Applicant's amendment and remarks.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3 , 4, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumagai et al. (US Patent Application Publication US 2002/0115622, published 22 Aug 2002, cited in PTO-892) in view of Koga et al. (Biol. Pharm. Bull., 2003, 26(9), p1299-1305, published online 06 Jun 2003, cited in PTO-892) and Mollica et al. (Journal of Pharmaceutical Sciences, 1978, 67(4), p443-465, cited in PTO-892).

Kumagai et al. discloses a pharmaceutical composition containing 2.0 g glycyrrhizin as the ammonium salt, 20.0 g aminoacetic acid, 1.0 g cysteine hydrochloride (page 3, paragraphs 48-54). In one embodiment this composition is dissolved in 1000 mL water (page 3, paragraphs 46), to give concentrations of 2.0 mg/mL glycyrrhizin as the ammonium salt, 20.0 mg/mL aminoacetic acid, and 1.0 mg/mL cysteine hydrochloride, addressing instant claims 1, 3, 4 and 10. Kumagai et al. discloses formulations may be manufactured using conventional arts (page 3, paragraph 36).

Kumagai et al. does not disclose the specific composition wherein the concentrations are 8 to 16 mg/mL of glycyrrhizin, 3 to 6 mg/mL of cysteine and 80 to 160 mg/mL of aminoacetic acid (instant claim 1). Kumagai et al. does not disclose a composition wherein the concentrations are 8 to 16 mg/mL of monoammonium glycyrrhizinate, 4 to 8 mg/mL of cysteine hydrochloride and 80 to 160 mg/mL of aminoacetic acid (instant claim 10). As convincingly argued, Kumagai et al. does not disclose a composition wherein substantially no sulfite is contained (instant claims 1, 3, 4, 9 and 10).

Koga et al. teaches a highly concentrated glyccyrhizin solution that is stable against precipitation as a gel (page 1299, right column, lines 3-10). Koga et al. teaches that a highly concentrated glyccyrhizin preparation is desirable because glyccyrhizin was detectable in plasma following oral administration of a large dose (page 1299, left column, lines 12-15). Koga et al. provides evidence that it is an expected result that an increased concentration of glycyrrhizin remains soluble, or stable, when in the presence of increased concentration of buffer (page 1301, right column, lines 4-10).

Mollica et al. teaches undesired "extrachemical" reactions can occur when stabilizing excipients are added to drug formulations (page 448, right column, lines 31-35). Mollica et al. teaches sodium bisulfite can cause precipitation of the drug from the formulation (page 449, left column, lines 2-3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the pharmaceutical composition containing ammonium glycyrrhizinate of Kumagai et al. with the increased concentration taught by Koga et al.

and the omission of sodium bisulfite taught by Mollica et al. Koga et al. teaches that a highly concentrated glyccyrhizin preparation is desirable because glyccyrhizin was detectable in plasma following oral administration of a large dose (page 1299, left column, lines 12-15) and provides evidence that it is an expected result that an increased concentration of glycyrrhizin remains soluble, or stable, when in the presence of increased concentration of buffer (page 1301, right column, lines 4-10). "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical." See MPEP 2144.05(II). As it is an expected result that an increased concentration of glycyrrhizin remains stable in the presence of increased concentration of buffer, no evidence is provided indicating the instantly claimed concentration range is critical. The function of sodium bisulfite is "stabilization due to sodium bisulfite", not stabilization in all aspects. The elimination of sodium bisulfite and the function of "stabilization due to sodium bisulfite" is obvious. See MPEP 2144.04(II)A. The function of "stabilization due to sodium bisulfite" is not desired because Koga et al. discloses the function of stabilization of an increased concentration of glycyrrhizin due to increased concentration of buffer. One would be motivated to eliminate sodium bisulfite because Mollica et al. teaches undesired "extrachemical" reactions can occur when stabilizing excipients are added to drug formulations (page 448, right column, lines 31-35), for example Mollica et al. teaches sodium bisulfite can cause precipitation of the drug from the formulation (page 449, left column, lines 2-3).

Instant claim 9 recites a property that is presumed to be inherent to the composition. As evidenced by the Merck Index (The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, 2006, Merck & Co., Inc., Whitehouse Station, NJ, USA, 14th Edition, cited in PTO-892), cysteine is freely soluble in water, alcohol, acetic acid, and ammonia water. Therefore, Kumagai et al. in view of Koga et al. and Mollica et al., in rendering instant claim 1 unpatentable as recited above also renders instant claim 9 unpatentable.

Response to arguments:

Applicant argues the criticality of the concentration of the invention by showing the claimed range achieves unexpected results, in that increased concentrations do not result in increased precipitation and degradation as disclosed in Table 2 of the instant specification. However, such a result is not an unexpected difference between the claimed invention and the prior art, as evidenced by Koga et al. (Biol. Pharm. Bull., 2003, 26(9), 1299-1305, cited in PTO-892). Koga et al. provides evidence that an increased concentration of glycyrrhizin remains soluble in the presence of increased concentration of buffer (page 1301, right column, lines 4-10). Cysteine hydrochloride and aminoacetic acid function as buffers, therefore it is expected that an increased concentration of glycyrrhizin would remain soluble in the presence of increased concentration of buffers.

Applicant argues the absence of sulfites would not have been obvious over the cited reference because the function of sulfites is as a stabilizer, and the function of stabilization is retained in the absence of the sulfites. Omission of the element with

retention of the element's function is indicia of unobviousness. However, the function of sulfites is "stabilization due to sulfites". As evidenced by Koga et al. above, the result that an increased concentration of glycyrrhizin remains soluble in the presence of increased concentration of buffer is known in the prior art. Therefore the composition with an increased concentration of glycyrrhizin as well as buffer is stabilized by the increased concentration of said components. Therefore the stabilization is caused by the increased concentration of buffer, and the function of "stabilization due to sulfites" is eliminated by omission of the sulfites.

With regard to the cited reference, US Patent 6,872,709, the translation of the publication of the Japanese application to which US Patent 6,872,709 claims foreign priority, Japanese Laid-Open Publication No. 2001-206849, by itself is not convincing, because US Patent 6,872,709 is not itself a translation or English-language equivalent of the foreign priority document. However, the US Patent 6,872,709 discloses the composition is the product High Efficiency Kaneo-Minofagen C made by Minofagen Pharmaceutical Industries Co. The majority of the evidence supports the finding that the composition as disclosed in US Patent 6,872,709 further contains sodium sulfite.

Conclusion

No claim is found to be allowable.

This Office Action modifies grounds of rejection not necessitated by Applicant's amendment. Accordingly, this action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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